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10/583,804	01/23/2007	Chunlin Tao	252846	4887

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EXAMINER	
SHTERENGARTS, SAMANTHA L	
ART UNIT	**PAPER NUMBER**
1626	

MAIL DATE	DELIVERY MODE
02/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,804	TAO ET AL.	
	Examiner	Art Unit	
	Samantha L. Shterengarts	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-76* is/are pending in the application.

4a) Of the above claim(s) *54,55 and 62-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-42, 47-48, 56-61, and 72-76* is/are rejected.

7)☒ Claim(s) *43-46 and 49-53* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-36 are cancelled. Claims 37-53, 56-61, 72, and new claims 73-76 are currently pending. Claims 54-55 and 62-71 are withdrawn for being drawn to a non-elected invention.

Response to Amendment

2. All rejections not explicitly maintained herein are withdrawn.

New Rejection – Necessitated by Amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

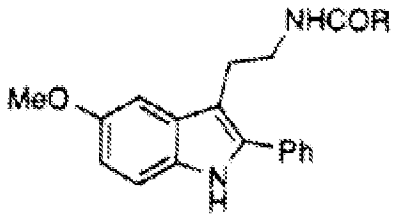
3. Claims 37-42, 47-48, 56-61, and 72-76 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Garratt et al. [Garratt, Peter J, *Mapping the Melatonin Receptor. 3. Design and Synthesis of Melatonin Agonists and Antagonists Derived from 2-Phenyltryptamines*, Journal of Medicinal Chemistry, 38(7) (1995), 1132-1139], in view of Patani et al. [Patani, George A. Bioisosterism: A rational approach in drug design. *Chem. Rev.* 96 (1996) 3147-3176.]

Determination of the scope and contents of the prior art

Garratt et. al. discloses obvious variants of the instantly claimed compounds.

Ascertaining the differences between the instant claims and the prior art

The following compounds are taught by Garratt et al.



compound	R	receptor binding [K_i], nM	*Xenopus* melanophores action, [conc], M
melatonin		0.59 ± 0.06	agonist, [10^{-8}]
6a	Me	0.0596 ± 0.0074	agonist, [10^{-8}]
6b	Et	0.0466 ± 0.0066	agonist, [10^{-8}]
6c	Prop	0.0558 ± 0.012	agonist, [10^{-8}]
6e	c-C_3H_5	0.3047 ± 0.066	agonist, [10^{-8}]
6f	c-C_4H_7	2.7 ± 0.66	agonist, [10^{-6}]
6g	c-C_5H_9	32.8 ± 7.8	agonist, [10^{-6}]
6h	c-C_6H_{11}	216 ± 31	agonist, [10^{-6}]

The following obvious modifications for compounds 6a, 6b, 6c, 6e, 6f, 6g, and 6h above all occur on the benzene ring of the indole: H v. F isosteric substitution at any R_1 substituent position. The instant claims teach R_1 as any halogen, and many of its species are drawn to R_1 being fluorine. The prior art reference teaches hydrogen in this position.

Garratt et al. also discloses pharmaceutical compositions for use as melatonin receptors and the design and synthesis of melatonin agonists and antagonists.

For instant claims 73-76, the identical modification occurs where R_2 can be a substituted aryl, specifically a substituted phenyl, which can be substituted by fluorine, an isosteric substitution to the hydrogen taught in the prior art reference.

Resolving the level of ordinary skill in the pertinent art – Prima facie case of obviousness

MPEP 2144.08.II.A.4(c) states, "…consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties."

With regards to the substitution of H and F, Patani et al. teaches the substitution of hydrogen by fluorine as a commonly employed monovalent isosteric replacement in rational drug design (pg. 3149).

One of ordinary skill would be motivated, from the disclosure in the prior art, to make the modifications required to arrive at the instant invention with reasonable expectation of success for obtaining a compound with the same utility. The motivation to make the change would be to make additional compound for the quoted purpose as taught by the prior art.

Thus, the instant claims are *prima facie* obvious.

4. Claims 37-40, 47-48, 56-61 and 72-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al., [Chen, Jia Jun, *Synthesis of 2-Iodo and 2-Phenyl-[^{11}C]melatonin: Potential PET Tracers for Melatonin Binding Sites*, Applied Radiation and Isotopes, 49(12) (1998), 1573-1579], in view of Patani et al. [Patani, George A. Bioisosterism: A rational approach in drug design. *Chem. Rev.* 96 (1996) 3147-3176.]

Determination of the scope and contents of the prior art

Chen et. al. discloses obvious variants of the instantly claimed compounds.

Ascertaining the differences between the instant claims and the prior art

The following compounds are taught by Chen et al.: Page 1577, Fig. 5, Compound 1b.

The following obvious modifications for compound 1b occur on the benzene ring of the indole: H v. F isosteric substitution at any R_1 substituent position. The instant claims teach R_1 as any halogen, and many of its species are drawn to R_1 being fluorine. The prior art reference teaches hydrogen in this position.

For instant claims 73-76, the identical modification occurs where R_2 can be a substituted aryl, specifically a substituted phenyl, which can be substituted by fluorine, an isosteric substitution to the hydrogen taught in the prior art reference.

Resolving the level of ordinary skill in the pertinent art – Prima facie case of obviousness

See discussion in section 3 above.

5. Claims 37-42, 47-48, 56-61, and 72-76 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Spadoni et al., [Spadoni, Gilberto, *2-Substituted 5-Methoxy-N-acyltryptamines: Synthesis, Binding Affinity for the Melatonin Receptor, and Evaluation of the Biological Activity*, Journal of Medicinal Chemistry, 36, (1993), 4069-4074.], in view of Patani et al. [Patani, George A. Bioisosterism: A rational approach in drug design. *Chem. Rev.* 96 (1996) 3147-3176.]

Determination of the scope and contents of the prior art

Spadoni et. al. discloses obvious variants of the instantly claimed compounds.

Ascertaining the differences between the instant claims and the prior art

The following compounds are taught by Spadoni et al.: Page 4070, compounds 4d and 4g.

The following obvious modifications for compounds 4d and 4g occur on the benzene ring of the indole: H v. F isosteric substitution at any R_1 substituent position. The instant claims teach R_1 as any halogen, and many of its species are drawn to R_1 being fluorine. The prior art reference teaches hydrogen in this position.

For instant claims 73-76, the identical modification occurs where R_2 can be a substituted aryl, specifically a substituted phenyl, which can be substituted by fluorine, an isosteric substitution to the hydrogen taught in the prior art reference.

Resolving the level of ordinary skill in the pertinent art – Prima facie case of obviousness

See discussion in section 3 above.

6. Claims 37-40, 47-48, 56-61, and 72-76 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Sastre et al., [Sastre, J.A. Lopez, *Biological activity of melatonin and some analogous: geometrical and electrical requirements*, Journal of Molecular Structure (Thermochem) 53, (2001), 271-281], in view of Patani et al. [Patani, George A. Bioisosterism: A rational approach in drug design. *Chem. Rev.* 96 (1996) 3147-3176.]

Determination of the scope and contents of the prior art

Sastre et. al. discloses obvious variants of the instantly claimed compounds.

Ascertaining the differences between the instant claims and the prior art

The following compound is taught by Sastre et al.: Page 274, compound 1.

The following obvious modification for compound 1 occurs on the benzene ring of the indole: H v. F isosteric substitution at any R_1 substituent position. The instant claims teach R_1 as

any halogen, and many of its species are drawn to R_1 being fluorine. The prior art reference teaches hydrogen in this position.

For instant claims 73-76, the identical modification occurs where R_2 can be a substituted aryl, specifically a substituted phenyl, which can be substituted by fluorine, an isosteric substitution to the hydrogen taught in the prior art reference.

Resolving the level of ordinary skill in the pertinent art – Prima facie case of obviousness

See discussion in section 3 above.

7. Claims 37-40, 47-48, 56-61, and 72-76 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Rivara et al., [Rivara, Silvia, *Three-Dimensional Quantitative Structure—Activity Relationship Studies on Selected MT_1 and MT_2 Melatonin Receptor Ligands: Requirements for Subtype Selectivity and Intrinsic Activity Modulation*, Journal of Medicinal Chemistry, 46 (2003) 1429-1439.], in view of Patani et al. [Patani, George A. Bioisosterism: A rational approach in drug design. *Chem. Rev.* 96 (1996) 3147-3176.]

Determination of the scope and contents of the prior art

Rivara et. al. discloses obvious variants of the instantly claimed compounds.

Ascertaining the differences between the instant claims and the prior art

The following compound is taught by Rivara et al.: Page 1430, Table 1, compounds 1-10-4, 1-10-13, 1-10-17, 1-10-18, 1-10-19, 1-10-20, 1-10-21, and 1-10-22.

The following obvious modification for compound 1 occurs on the benzene ring of the indole: H v. F isosteric substitution at any R_1 substituent position. The instant claims teach R_1 as

any halogen, and many of its species are drawn to R_1 being fluorine. The prior art reference teaches hydrogen in this position.

For instant claims 73-76, the identical modification occurs where R_2 can be a substituted aryl, specifically a substituted phenyl, which can be substituted by fluorine, an isosteric substitution to the hydrogen taught in the prior art reference.

Resolving the level of ordinary skill in the pertinent art – Prima facie case of obviousness

See discussion in section 3 above.

8. Claims 37-40, 47-48, 56-61, and 72-76 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Mor et al., [Mor, Marco, *Synthesis, Pharmacological Characterization and QSAR Studies on 2-Substituted Indole Melatonin Receptor Ligands,* Bioorganic and Medicinal Chemistry, 9 (2001) 1045-1057.], in view of Patani et al. [Patani, George A. Bioisosterism: A rational approach in drug design. *Chem. Rev.* 96 (1996) 3147-3176.]

Determination of the scope and contents of the prior art

Mor et. al. discloses obvious variants of the instantly claimed compounds.

Ascertaining the differences between the instant claims and the prior art

The following compound is taught by Mor et al.: Page 1047, Table 1, compound 9.

The following obvious modification for compound 9 occurs on the benzene ring of the indole: H v. F isosteric substitution at any R_1 substituent position. The instant claims teach R_1 as any halogen, and many of its species are drawn to R_1 being fluorine. The prior art reference teaches hydrogen in this position.

For instant claims 73-76, the identical modification occurs where R_2 can be a substituted aryl, specifically a substituted phenyl, which can be substituted by fluorine, an isosteric substitution to the hydrogen taught in the prior art reference.

Resolving the level of ordinary skill in the pertinent art – Prima facie case of obviousness

See discussion in section 3 above.

9. Claims 37-40, 47-48, 56-61, and 72-76 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Ito et al., [Ito, Satoru, *Acetone-Sensitized Photocoupling of 5-Bromouridine to Tryptophan Derivatives via Electron-Transfer Process*, Journal of American Chemical Society, 102 (1980) 7535-754.], in view of Patani et al. [Patani, George A. Bioisosterism: A rational approach in drug design. *Chem. Rev.* 96 (1996) 3147-3176.]

Determination of the scope and contents of the prior art

Ito et. al. discloses obvious variants of the instantly claimed compounds.

Ascertaining the differences between the instant claims and the prior art

The following compound is taught by Ito et al.: Page 7539, scheme 4, compound 19.

The following obvious modification for compound 19 occurs on the benzene ring of the indole: H v. F isosteric substitution at any R_1 substituent position. The instant claims teach R_1 as any halogen, and many of its species are drawn to R_1 being fluorine. The prior art reference teaches hydrogen in this position.

Resolving the level of ordinary skill in the pertinent art – Prima facie case of obviousness

See discussion in section 3 above.

Claim Objections

10. Claims 43-46 and 49-53 are objected to for depending on a rejected base claim.

Conclusion

11. No claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samantha Shterengarts whose telephone number is (571)270-5316. The examiner can normally be reached on Monday thru Thursday 9-6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samantha L. Shterengarts/
Examiner, Art Unit 1626

/Kamal A Saeed/
Primary Examiner, Art Unit 1626